Offic Action Summary	Application No. 09/918,637	Applicant(s) JEHANLI ET AL.	
	Examin r Ja-Na Hines	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☒ Claim(s) *5-7,9,12,15-17 and 19-21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse in Paper No. 7 is acknowledged. Claims 1-21 including species drawn to rabbit serum albumin and lisinopril are under consideration in this office action.

Drawings

2. The drawings were received on August 1, 2001 are acceptable.

Specification

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. The language should be clear and concise and should not repeat information given in the title.

4. The use of the trademark TWEEN-20™ and other reagents have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

5. Claims 5-7, 9, 12, 15-17 and 19-21 are objected to under 37 CFR 1.75(c) as being in improper dependent form because a multiple dependent claim should not depend from another multiple dependent claim. See MPEP § 608.01(n). Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 refers to a first part and second part, however it is unclear what parts of the kit the first and second part comprise.

Claim 1 is drawn to a second part containing a labeled anti-drug antibody; it is unclear whether this antibody is the specific binding partner of the drug conjugate or of some undisclosed drug.

Also, the claim is unclear as to whether the antibody is labeled with gold material and latex particles as indicated by the alternative language of the claim. Therefore the metes and bounds of the claims are unclear and clarification is requested.

7. Claims 5-7, 9, 12, 15-17 and 19-21 are indefinite. The claims are indefinite because one will not know from which claim the claims depend. Thus, the metes and

bounds of the claim cannot be ascertained. See also the objection to the claims. Clarification is requested.

It is noted that the claims are viewed as depending from claim 1.

8. Claims 2 and 6 recite the limitation "said drug" in the claims. There is insufficient antecedent basis for this limitation in the claim.

9. Claim 9 is unclear, the claim is drawn to an interior at least partially coated therewith, however, it is unclear what the interior is coated with, i.e., is it antibodies or something else. Clarification is required to overcome the rejection.

10. The term "maximum binding" in claim 12 is a relative term which renders the claim indefinite. The term "maximum binding" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the claims cannot be ascertained since it is unclear how to determine maximum binding when there is nothing to compare the binding to. Therefore clarification is required to overcome the rejection.

11. Claims 11 and13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A

trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a particular material, i.e. NUNC-IMMUNO ^{TM} STICK and accordingly the identification is indefinite. Furthermore, the use of trademarks is improper since products identified by trademarks are within the sole control of the trademark owner and are subject to change by said owner at their discretion.

12. Claims 16-21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. There are no method steps recited in the claims. The omitted steps are: there is no contact step which would allow for the qualitative or quantitative determination of a drug in a fluid. There is no detect step which would allow one to detect the drug and there is not correlation step between the detection and the qualitative or quantitative determination of a drug in a fluid.

Moreover, the preamble of claim 16 is drawn to a method for qualitative or quantitative determination of a drug in a fluid, however the preamble of the claim must be drawn to the same method steps that are recited by the body of the claims. The preamble is inconsistent since the body of the claim fails to recite method steps that would teach how to make a qualitative or quantitative determination of a drug in a fluid. Therefore, the claim is incomplete because it lacks any steps for such determinations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-3, 5-10, 12 and 14-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jehanli et al., (1996) and Baker et al., in view of Cole et al., (US Patent 4,589,612).

The claims are drawn to a medical kit for qualitative or quantitative determination of a drug in a biological fluid comprising a first part coated with a drug conjugate and a second part that contains a labeled anti-body and is adapted for receiving said fluid. Additional claims are drawn to a method for qualitative or quantitative determination of a drug in a biological fluid comprising a first part and a labeled anti-drug antibody.

Jehanli et al., (1996) teach determination of Captopril in human blood by an ELISA assay. Captopril is an orally active Angiotension-Converting Enzyme (ACE) inhibitor used for treatment of hypertension and congestive heart failure (page 914). The quantitation of Captopril in biological fluids has been carried out previously in the art, however the author describes the development of a sensitive, simple and rapid competitive ELISA assay for the determination of captopril (page 914). Captopril was covalently linked to bovine serum albumin (page 914). Antibodies were created from the immunization protocol (page 915). Preparation of rabbit serum albumin (RSA)-captopril conjugate for the immunoassay was disclosed (page 915). Figure 1 shows chemical

coupling of captopril to both bovine serum albumin and rabbit serum albumin. The microtiter plate immunoassay consisted of coupling captopril to RSA using well-known general procedures already described (page 915). The microtitre strips were coated by incubation with the RSA-captopril (page 915). Thus, this first part is coated with the drug conjugate, rabbit serum albumin. Anti-captopril antibody was added to the tube shaped wells and strips (page 915). Thus, this second part contains labeled antibody and is adapted for receiving the biological fluid. The strips were incubated for one hour at ambient temperatures and the washed bound antibody was revealed (page 915). Color development was terminated and the absorbance was determined (page 915). Human plasma samples containing various concentrations of captopril were tested and amounts of captopril was qualitatively or quantitatively determined (page 915). Maximum absorbance values and concentration of captopril in test samples was determined. Jehanli et al., teach both the medical kit and methods of using the kit to determine the presence of a drug. However, Jehanli et al., do not teach the use of Lisinopril.

Baker et al., teach that ACE inhibitors refer to angiotension-converting enzyme inhibiting drugs which prevent the conversion of angiotension I to angiotension II (col. 15 lines 47-50). The ACE inhibitors may be beneficial in congestive heart failure by reducing systemic vascular resistance and relieving circulatory congestion (col. 15 lines 50-53). ACE inhibitors include the generic drugs known as captopril and lisinopril (col. 15 lines 55-57). However, Baker et al., do not teach the use of gold material particles.

Cole et al., (US Patent 4,589,612) teach immunoassays using labeled radioisotopes or enzymes as color formers (col.1-2 lines 55-35). Such immunoassays can utilize a labeled component comprising a metal containing particle of a size and character to facilitate the maintenance of a generally stable, monodispersed suspension of the labeled component that was mixed and brought into contact with the sample to be analyzed (col. 4-5 lines 60-5). The labeled component can be an antibody labeled with metal particles such as gold sol particles which have been known in the art since 1975. Gold particles coated with antibody are intensely colored orange, red or violet depending on particle size (col. 6-7 lines 60-2). The gold labeled antibodies can be directly visualized with the naked eye (col. 7 lines 8-11). Moreover metal sol assays require fewer steps and fewer reagents and are considered more stable than most enzyme labeled antibodies (col. 7 lines 13-16). The particles can be used with either monoclonal or polyclonal antibodies (col. 8 lines 12-13). Moreover, such immunoassays can be used to detect controlled substances and other such small molecules (col. 9 lines 1-3).

Jehanli et al., Baker et al., and Cole et al., teach a medical kit comprised of microstrips coated with drug conjugate, lisinopril-RSA, this is the first part is coated with the drug conjugate and having a second part which contained gold material labeled anti-drug antibody wherein wells were adapted for receiving sample as claimed. Therefore the prior art teaches the medical kit.

It would have been prima facie obvious to modify the medical kit for qualitative or quantitative determination of a drug in a biological fluid comprising a first part coated with a drug conjugate and a second part that contains a enzyme labeled antibody and is adapted for receiving said fluid as taught by Jehanli et al., wherein no more than routine skill would have been required to incorporate the lisinopril drug conjugate and gold labeled antibody of Baker et al., and Cole et al. One would have a reasonable expectation of success by incorporating the ACE drug lisinopril, when the prior art already teaches the determination of another ACE related drug which has similar functions and using an antibody labeled with gold material, into the device and method of Jehanli et al., who already teach using the labeled antibodies to qualitatively or quantitatively determine the presence of a drug in a biological fluid. Moreover, no more than routine skill would have been required to use an alternative yet functionally equivalent drug and labeled antibody in the medical kit and method of determination as taught by Jehanli et al., since only the expected results would have been obtained. A skilled artisan would have had a reasonable expectation of success in switching the ACE inhibitor drugs where the prior art already using one ACE drug can be detected and similar drugs are readily available. Thus the use of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on the gold labeled antibody ability to be linked with either monoclonal or polyclonal antibodies, its ability to be directly visualized, and its very stable nature when compared to enzyme labels.

14. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jehanli et al., (1996), Baker et al., and Cole et al., (US Patent 4,589,612) further in view of de Jaeger et al., (US Patent 4,837,168).

The claim is drawn to a medical kit for qualitative or quantitative determination of a drug in a biological fluid comprising a first part coated with a conjugated drug, and a second part that contains an antibody with colored latex particles and is adapted for receiving said fluid. The prior art has been discussed above, however none teaches using colored latex particles.

de Jaeger et al., teach a method of qualitatively or quantitatively determining a component of a complex formed between at least one specific binding agent and its corresponding bindable substance (col. lines 20-24). The color signal may be easily detected and optionally quantified either directly or if necessary after development (col. 2 lines 40-43). The optical properties of latex particles especially their color characteristics make them optimal labels (col. 2 lines 50-56). Examples of colored or colorable latex particles are well known in the art (col. 3-5 lines 10-40). Example 1 teaches the preparation of latex bound antibodies, performance of coupled latex wherein nitrocellulose strips were incubated with latex suspensions and color was then developed (col. 17-18 lines 62-68). The detection sensitivity and specificity was determined along with designing a dipstick, see example 2.

It would have been prima facie obvious to modify the medical kit for qualitative or quantitative determination of a drug in a biological fluid comprising a first part coated with a drug conjugate and a second part that contains a labeled antibody and is adapted

for receiving said fluid as taught by Jehanli et al., and Cole et al., to include the colored latex particle label as taught by de Jaeger et al. One would have a reasonable expectation of success by incorporating the antibody labeled with latex colored particles, into the device of Jehanli et al., and Cole et al., who already teach using the labeled antibodies to qualitatively or quantitatively determine the presence of a drug in a biological fluid. Moreover, no more than routine skill would have been required to use an alternative yet functionally equivalent labeled antibody in the medical kit as taught by Jehanli et al., and Cole et al., since only the expected results would have been obtained; thus the use of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on colored latex particle labeled antibodies being known to be capable of direct visualization and useable in dipstick immunoassay supports to qualitatively or quantitatively determine the presence of an antigen.

15. Claims 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jehanli et al., (1996) Baker et al., and Cole et al., (US Patent 4,589,612) in further view of Esser. The prior art has been discussed above, however none teaches using the NUNC-IMMUNO ^{TM} STICK.

The claims drawn to a medical kit for qualitative or quantitative determination of a drug in a biological fluid comprising a first part coated with a drug conjugate that has the shape and material of a NUNC-IMMUNO ^{TM} STICK and a second part that contains a labeled anti-body and is adapted for receiving said fluid.

Esser teaches NUNC-IMMUNO ™ STICK. The immunosticks can be used for assaying one or two analytes with controls at the same time and can be used in the doctor's office or in the field. Assays testing one analyte use rabbit immunoglobulin IgG in a double antibody sandwich assay using anti-rabbit antibodies conjugated with alkaline phosphatase (page 4). MaxiSorp sticks were coated with labeled antibody, alkaline phosphatase conjugated swine anti-rabbit antibodies (page 4). See Figure 1 wherein the immunostick ELISA of the analyte was performed. The NUNC-IMMUNO ™ STICK test systems consist of a tube and stick with a paddle.

It would have been prima facie obvious to modify the medical kit for qualitative or quantitative determination of a drug in a biological fluid comprising a first part coated with a drug conjugate and a second part that contains a labeled antibody and is adapted for receiving said fluid as taught by Jehanli et al., and Cole et al., to further incorporate the shape and material used in NUNC-IMMUNO ™ STICK test system. One would have a reasonable expectation of success by incorporating the NUNC-IMMUNO ™ STICK test system because it can assay multiple anaytes wherein both positive and negative controls are run at the same time on one immunostick and can be used in a doctors office. Moreover, no more than routine skill would have been required to use an alternative yet functionally equivalent immunostick as compared to the immunostrips as taught by Jehanli et al., and Cole et al., since only the expected results would have been obtained; thus the use of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on the ease and commercial availability of the NUNC-IMMUNO ™ STICK test system.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines
June 18, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
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